PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 66054010PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/25332	International filing date *(day/month/year)* 06 August 2004 (06.08.2004)	Priority date *(day/month/year)* 06 August 2003 (06.08.2003)
International Patent Classification (IPC) or national classification and IPC IPC: Please See Continuation Sheet USPC: 216/2;250/307;252/518.1;435/4;438/14;528/380		
Applicant IMAGO SCIENTIFIC INSTRUMENTS CORPORATION		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 4 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21 October 2005 (21.10.2005)	21 June 2006 (21.06.2006)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Susan E. Fernandez Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/25332

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

☐ the international application in the language in which it was filed.

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4(a))

☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-44 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages NONE as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* 45-48 received by this Authority on 21 October 2005 (21.10.2005)
pages* NONE received by this Authority on _____

☒ the drawings:
pages 1/20-20/20 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☒ the claims, Nos. 29
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/25332

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 2-12,15,16,18,19,23 and 24	YES
	Claims 1,13,14,17,20-22 and 25-28	NO
Inventive Step (IS)	Claims 8-11,15,18,23	YES
	Claims 1-7,12-14,16,17,19-22 and 24-28	NO
Industrial Applicability (IA)	Claims 1-28	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)
Please See Continuation Sheet

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of:

Continuation of IPC:
C08G 75/00(2006.01);**C12Q 1/00**(2006.01);**C23F 1/00**(2006.01);**G01N 23/00**(2006.01);**G01R 31/26**(2006.01);**G21K 7/00**(2006.01);**H01B 1/02**(2006.01),**1/08**(2006.01);**H01L 21/66**(2006.01)

V. 2. Citations and Explanations:
Claims 1, 13-14, 17, 20-22, and 25-28 lack novelty under PCT Article 33(2) as being anticipated by Kelly et al. (US 2001/0044156 A1). Kelly et al. teaches methods of sampling specimens for microanalysis wherein a study specimen is embedded in a larger study object (the matrix) to yield an embedded specimen. Focused ion beam lithography may be used, and biological materials may be applied. The prepared specimen is well suited for atom probe microanalysis. Thus, the above claims are anticipated.

Claims 1-6, 12-14, 16, 17, 19-22, and 24-28 lack an inventive step under PCT Article 33(3) as being obvious over Kelly et al. (US 2001/0044156 A1) in view of Ban et al. Kelly et al. teaches methods of sampling specimens for microanalysis wherein a study specimen is embedded in a larger study object (the matrix) to yield an embedded specimen. Focused ion beam lithography may be used, and biological materials may be applied. The prepared specimen is well suited for atom probe microanalysis. Kelly et al. does not require that the study specimen is embedded within a polymer matrix. Ban et al. teaches the development of multi-phase polymer blends wherein osmium tetroxide and ruthenium tetroxide staining is applied, which aids in the detection of polymer domains. It would have been obvious to one of ordinary skill in the art to have modified the Kelly invention such that the matrix is treated as discussed in Ban et al., since the methods of Ban et al. allowed for successful detection of polymer domains. Moreover, the presence of osmium tetroxide and ruthenium tetroxide staining inherently increases the conductivity of the polymer matrix.

Claims 1-7, 12-14, 16, 17, 19-22, and 24-28 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in last paragraph and further in view of van der Linden et al. Kelly et al. and Ban et al. do not disclose embedding the specimen in hydrogel. van der Linden et al. discloses fabrication of hydrogels with photopatterns. It would have been obvious to one of ordinary skill in the art to have modified the invention rendered obvious by Kelly et al. and Ban et al. such that the specimen is embedded in hydrogel, since hydrogel is highly flexible and is easy to manufacture.

Supplemental Box

Claims 8-11, 15, 18, and 23 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the process by which the specimen is embedded within the electrically conductive polymer matrix, a polymer matrix comprising polythiophenes, polyanilines, or polypyrroles, doping the embedded specimen or specimen-coated substrate, or the stabilization of the specimen by cross-links.

Claims 1-28 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

With regard to applicant's amendments/remarks filed October 21, 2005, it is noted that the polymer matrix of Ban et al. would have been a suitable, electrically conductive matrix for embedding the specimen since its domains are detectable, which would mean that any specimen embedded in the detectable polymer domain would also have been detectable based on the polymer domain. Though Ban et al. does not teach embedding a specimen in a matrix or the forming regions on the embedded specimen into shapes suitable for microanalysis by an atom probe, Kelly et al. teaches these embodiments. With regard to the arguments that the polymer matrix of Ban et al. is not treated to increase its conductivity, it is respectfully noted that Ban et al. teaches treating the polymer matrix with osmium tetroxide and ruthenium tetroxide, which inherently increases the conductivity of the polymer matrix.

---------- NEW CITATIONS ----------

CLAIMS

What is claimed is:

1. A method of preparing a specimen for microanalysis, the method comprising:

(a) embedding the specimen within an electrically conductive polymer matrix to yield an embedded specimen; and

(b) forming regions on the embedded specimen into shapes suitable for microanalysis by an atom probe.

2. The method of claim 1, wherein in step (a), the specimen is embedded within an intrinsically conductive polymer matrix.

3. The method of claim 1, wherein in step (a), the specimen is embedded within a polymer matrix and further comprising a step of treating the polymer matrix to increase its conductivity.

4. The method of claim 3, wherein the polymer matrix is treated with a metal-containing compound, wherein the treatment increases the conductivity of the polymer matrix.

5. The method of claim 3, wherein the polymer matrix is treated with a metal-containing compound selected from a group consisting of osmium-containing compounds and ruthenium-containing compounds.

6. The method of claim 3, wherein the polymer is treated with a metal-containing compound selected from a group consisting of osmium tetroxide and ruthenium tetroxide.

7. The method of claim 1, wherein in step (a), the specimen is embedded within a hydrogel.

8. The method of claim 1, wherein in step (a), the specimen is embedded within the electrically conductive polymer matrix by mixing the specimen with a corresponding monomeric compound and then polymerizing the monomeric compound to yield the electrically conductive polymer matrix.

9. The method of claim 1, wherein in step (a), the specimen is embedded within the electrically conductive polymer matrix by mixing the specimen with a corresponding pre-polymer compound and then polymerizing the pre-polymer compound to yield the electrically conductive polymer matrix.

10. The method of claim 1, wherein in step (a), the specimen is embedded within the electrically conductive polymer matrix by mixing the specimen with a corresponding water-soluble monomeric compound and then polymerizing the monomeric compound in aqueous solution to yield the electrically conductive polymer matrix.

11. The method of claim 1, wherein in step (a), the specimen is embedded within a matrix comprising a polymer selected from a group consisting of polythiophenes, polyanilines, polypyrroles, and combinations thereof.

12. The method of claim 1, wherein in step (a), the embedded specimen is disposed on a substrate prior to step (b).

13. The method of claim 1, wherein in step (a), the embedded specimen is disposed on a substrate after step (b).

14. The method of claim 1, wherein in step (b), the regions are formed using focused ion beam lithography.

15. The method of claim 1, wherein in step (b), the regions are formed by doping the embedded specimen with a masking agent and then exposing the embedded specimen to a broad ion beam under conditions and for a time sufficient to remove the masking agent from the embedded

specimen, whereby regions protruding from embedded specimen and suitable for microanalysis by an atom probe are formed.

16. The method of claim 1, wherein in step (a), the embedded specimen is disposed on a substrate prior to step (b) to yield a specimen-coated substrate, and then, in step (b), forming regions on the specimen-coated substrate suitable for microanalysis by an atom probe.

17. The method of claim 16, wherein in step (b), the regions are formed using focused ion beam lithography.

18. The method of claim 1, wherein in step (b), the regions are formed by doping the specimen-coated substrate with a masking agent and then exposing the specimen-coated substrate to a broad ion beam under conditions and for a time sufficient to remove the masking agent from the embedded specimen, whereby regions protruding from embedded specimen and suitable for microanalysis by an atom probe are formed.

19. The method of claim 1, wherein in step (a), an organic or biological specimen is embedded within the matrix.

20. The method of claim 1, wherein a protein is embedded within the matrix.

21. The method of claim 1, further comprising the steps of forming regions on a substrate suitable for microanalysis by an atom probe, and immobilizing the embedded specimen on the formed regions of the substrate, whereby regions on the embedded specimen are formed into shapes suitable for microanalysis by an atom probe.

22. The method of claim 1, further comprising the steps of forming regions on a substrate suitable for microanalysis by an atom probe, and immobilizing the specimen on the formed regions of the substrate, and then

coating the formed regions of the substrate with the electrically conductive matrix, whereby the specimen is embedded within the matrix.

23. The method of claim 1, further comprising stabilizing the specimen by forming internal cross-links within the specimen, by forming cross-links between the specimen and the matrix, by forming cross-links between the specimen and a substrate, or combinations thereof.

24. The method according to any one of the preceding claims, further comprising step (c): and then microanalyzing the shapes formed in step (b).

25. The method of claim 24, wherein in the shapes are microanalyzed by atom probe microscopy.

26. The method of claim 24, wherein in the shapes are microanalyzed by local electrode atom probe microscopy.

27. An atom probe specimen fabricated by a method according to any one of claims 1 to 24.

28 A composition of matter comprising an intrinsically conductive polymer whose conductivity has been altered by contact with a compound selected from a group consisting of osmium tetroxide, ruthenium tetroxide, and combinations thereof.